PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 306459WO/JND/CG	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/GB2004/003201	International filing date *(day/month/year)* 23.07.2004	Priority date *(day/month/year)* 23.07.2003
International Patent Classification (IPC) or national classification and IPC C12N15/10, C12Q1/68, G01N33/50		
Applicant CYCLOPS GENOME SCIENCES LIMITED et al.		

1. This report is the International preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the International application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☒	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the International application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
10.02.2005	11.07.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Bradbrook, D Telephone No. +49 89 2399-7413

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/003201

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages	
1-30	as originally filed
Claims, Numbers	
1-39	as originally filed
Drawings, Sheets	
1/2-2/2	as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/003201

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	10,19-21,23-32,34-39
	No:	Claims	1-9,11-18,22,33
Inventive step (IS)	Yes:	Claims	23-32
	No:	Claims	1-22,33-39
Industrial applicability (IA)	Yes:	Claims	1-39
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Section V

1 Reference is made to the following documents:

D1: BAKER ET AL: "Enantiomeric resolution of tris-1 10-phenanthrolineruthenium ion and bis-2 2'-bipyridineruthenium 4' 7'-phenanthrolino-5' 6' 5 6-pyrazine ion on a DNA hydroxylapatite column" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol. 113, no. 4, 1991, pages 1411-1412

D2: ALDRICH-WRIGHT ET AL: "Development of DNA-immobilised chromatographic stationary phases for optical resolution and DNA-affinity comparison of metal complexes" JOURNAL OF CHROMATOGRAPHY A, vol. 718, no. 2, 22 December 1995, pages 436-443

D3: WO 90/10637 A (DU PONT) 20 September 1990

D4: WO 00/75302 A (GOLDSBOROUGH ANDREW SIMON ; CYCLOPS GENOME SCIENCES LTD (GB)) 14 December 2000

D5: LABROU N ET AL: "The affinity technology in downstream processing" JOURNAL OF BIOTECHNOLOGY, vol. 36, no. 2, 15 August 1994, pages 95-119

D6: WO 2004/013155 A (GOLDSBOROUGH ANDREW SIMON ; CYCLOPS GENOME SCIENCES LTD (GB)) 12 February 2004

2 Novelty (Art.33(2) PCT)

2.1 Claim 1 is directed to a material for separating two components of a mixture (cf item VIII.1) and is defined in functional terms, namely such that the solid phase is capable of binding one component and the coating covers the solid phase to such an extent as to impede binding of the other component to the solid phase. These features allow a very broad interpretation: the respective components are not defined; they way in which the coating impedes binding of the analyte to the solid phase is not defined; the extent of coating required to impede said binding is not defined. Furthermore, the nature of the binding is not defined.

2.2 A number of different matrices used routinely in methods for separation of components in a mixture fall within the scope of claim 1. In particular, a number of

polymeric solid phases such as agarose, acrylamide and polycarbonate or mineral solid phases such as silica, metals, glass and hydroxylapatite, are routinely coated or derivatised such as to allow preferential binding of one or more components in a mixture, leaving others in solution. Ion-exchange media such as DEAE-cellulose comprise a solid phase coated with charged particles which prevent binding of molecules having the same charge that would be capable, in the absence of the coating, of binding the solid phase. Other examples include matrices used in affinity chromatography or solid phases used in specific binding assays (e.g. antibodies bound to agarose beads; oligonucleotides bound to latex articles; streptavidin immobilized on polystyrene plates). The range of such supports is illustrated by D5 and particular examples are given below; many such materials such as those already mentioned are so common in the art that specific prior art documents are unnecessary.

2.3 In particular embodiments, DNA has been immobilised on hydroxylapatite for affinity chromatographic purposes (e.g. D1, D2). D3 discloses a silane-treated silica gel (cf Example 1), which can be used to remove protein from a DNA solution. D4 discloses 2'-OH-modified RNA immobilized on silica particles (e.g. Example 8). Embodiments covered by the product claims include, for instance, hydroxylapatite coated with polynucleotides (cf claims 6 and 13). As the extent of coating required by the claims is not defined, this feature cannot distinguish such claimed subject-matter from the prior art. As such, the definition of this embodiment is merely that the material comprises hydoxylapatite as a solid phase coated with polynucleotide molecules. This is not novel over D1.

2.4 It should be noted that, with respect to the present product claims, the way in which the materials are used in the prior art is irrelevant, as long as the materials are suitable for the intended use stated in the claims.

2.5 Therefore, the subject-matter of claim 1 and dependent claims 2-9 and 11-18 is not novel. For the same reasons, claim 22 is also not novel.

2.6 The subject-matter of claim 33 is not novel over D3, which discloses the removal, using coated support materials, of proteins from mixtures containing nucleic acids.

Suitable supports include silica, cellulose and agarose (cf p.7, l.23 - p.8, l.14; Example 1E).

2.7 Claim 23 appears to be novel (Art.33(2) PCT) as the prior art does not disclose a method of using the materials discussed above whereby one constituent is separated by binding to the solid phase (i.e. not the coating) of the material whereas another component is prevented from binding thereto. It follows that dependent claims 24-32 are also novel.

2.8 The prior art does not disclose a kit as defined in claims 34-39, which claims are therefore novel (Art.33(2) PCT)

3 Inventive step (Art.33(3) PCT)

3.1 Magnetic hydroxylapatite is commercially available, as noted in the present description (p.8, para.2), and would be a routine option for the skilled person carrying out separation methods (cf also D4: p.23, para.2, relating to use of magnetic beads). Therefore, the subject-matter of claims 10, 20 and 21 does not involve an inventive step (it is noted that D1 and D2 use calf thymus DNA, which would have at least 50 nucleotides).

3.2 The further feature of dependent claim 19 is a routine feature that may be used according to needs, and therefore does not confer an inentive step on the claimed subject-matter.

3.3 The components of the kits defined in claims 34-39 appear to be well-known reagents that would be used in routine experimentation with the materials discussed in items 2.1-2.3 above. Therefore, and because the packaging into a kit itself does not confer inventive activity, the subject-matter of claims 34-39 is not considered to involve inventive activity.

3.4 The subject-matter of claims 23-32 would appear to involve an inventive step, as there is no suggestion in the prior art to use the materials in question in such a way as to bind a component of a mixture to the solid phase of a coated material, thereby

separating it from another component which is prevented by the coating from binding to the solid phase.

Section VI

1 The examination report has been based on an assumed valid priority for the present application. Should the priority of the present application not be valid, document D6 would be relevant with respect to novelty and inventive step (Article 33(2) and (3) PCT). Furthermore, should the present application enter the national or regional phase, D6 could be relevant to the question of novelty.

Section VIII

1 Claim 1 is unclear (Art.6 PCT), in that it seeks to define the material with respect to an analyte and an undesired constituent, neither of which is defined in any way. According to circumstances, an analyte in one system may be a contaminant in another. Therefore, claim 1 has been interpreted such that the analyte and undesired constituent are any two components to be separated in a mixture.